

IN THE CLAIMS:

Please cancel claims 1-18, 20, and 22-24.

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18. (CANCELED)

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19. (AMENDED) A method of identifying agonists to the IGS1 polypeptide of ~~claim 13~~ comprising an amino acid sequence that is at least 80% identical to the amino acid sequence of SEQ ID NO: 2 over its entire length, comprising:

(a) contacting a cell which produces a IGS1 polypeptide with a test compound;
and

(b) determining whether the test compound effects a signal generated by activation of the IGS1 polypeptide.

20. (ORIGINAL) An agonist identified by the method of claim 19.

21. (AMENDED) The method for identifying antagonists to the IGS1 polypeptide of ~~claim 13~~ comprising an amino acid sequence that is at least 80% identical to the amino acid sequence of SEQ ID NO: 2 over its entire length, comprising:

(a) contacting a cell which produces a IGS1 polypeptide with an agonist; and
(b) determining whether the signal generated by said agonist is diminished in the presence of a candidate compound.

22. (ORIGINAL) An antagonist identified by the method of claim 21.

23. (CANCELED)

24. (CANCELED)

25. (NEW) The method of claim 19 wherein the IGS1 polypeptide comprises an amino acid sequence identical to the amino acid sequence of SEQ ID NO: 2.

26 (NEW) The method of claim 21 wherein the IGS1 polypeptide comprises an amino acid sequence identical to the amino acid sequence of SEQ ID NO: 2.

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Claims

1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
 - 5 a) a nucleotide sequence encoding the IGS1 polypeptide according to SEQ ID NO: 2;
 - b) a nucleotide sequence encoding the polypeptide encoded by the DNA insert contained in the deposit no. CBS 102049 at the Centraalbureau voor Schimmelcultures at Baarn the Netherlands, in particular a nucleotide sequence
10 corresponding to the SEQ ID NO: 1;
 - c) a nucleotide sequence having at least 80 % (preferably at least 90%) sequence identity over its entire length to the nucleotide sequence of (a) or (b);
 - d) a nucleotide sequence which is complementary to the nucleotide sequence of (a) or (b) or (c).
15
2. The polynucleotide of claim 1 wherein said polynucleotide comprises the nucleotide sequence contained in SEQ ID NO:1 encoding the IGS1 polypeptide of SEQ ID NO:2.
3. The polynucleotide of claim 1 wherein said polynucleotide comprises a nucleotide
20 sequence that is at least 80% identical to that of SEQ ID NO:1 over its entire length.
4. The polynucleotide of claim 3 which is the polynucleotide of SEQ ID NO:1.
5. The polynucleotide of claim 1-4 which is DNA or RNA.
25
6. A DNA or RNA molecule comprising an expression system, wherein said expression system is capable of producing an IGS1 polypeptide comprising an amino acid sequence, which has at least 80% identity with the polypeptide of SEQ ID NO:2 when said expression system is present in a compatible host cell.
30
7. A host cell comprising the expression system of claim 6.
8. A host cell according to claim 7 which is a yeast cell
- 35 9. A host cell according to claim 7 which is an animal cell
10. IGS1 receptor membrane preparation derived from a cell according to claim 7-9.

AMENDED SHEET
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11. A process for producing an IGS1 polypeptide comprising culturing a host of claim 7 under conditions sufficient for the production of said polypeptide and recovering the polypeptide from the culture.
- 5 12. A process for producing a cell which produces an IGS1 polypeptide thereof comprising transforming or transfecting a cell with the expression system of claim 6 such that the cell, under appropriate culture conditions, is capable of producing an IGS1 polypeptide.
- 10 13. An IGS1 polypeptide comprising an amino acid sequence which is at least 80% identical to the amino acid sequence of SEQ ID NO:2 over its entire length.
14. The polypeptide of claim 13 which comprises the amino acid sequence of SEQ ID NO:2.
- 15 15. An antibody immunospecific for the IGS1 polypeptide of claim 13.
16. A method for the treatment of a subject in need of enhanced activity or expression of IGS1 polypeptide receptor of claim 13 comprising:
- (a) administering to the subject a therapeutically effective amount of an agonist to said receptor; and/or
- 20 (b) providing to the subject an isolated polynucleotide comprising a nucleotide sequence that has at least 80% identity to a nucleotide sequence encoding the IGS1 polypeptide of SEQ ID NO:2 over its entire length; or a nucleotide sequence complementary to said nucleotide sequence in a form so as to effect production of said receptor activity in vivo.
- 25 17. A method for the treatment of a subject having need to inhibit activity or expression of IGS1 polypeptide receptor of claim 13 comprising:
- (a) administering to the subject a therapeutically effective amount of an antagonist to said receptor; and/or
- 30 (b) administering to the subject a polynucleotide that inhibits the expression of the nucleotide sequence encoding said receptor; and/or
- (c) administering to the subject a therapeutically effective amount of a polypeptide that competes with said receptor for its ligand.
- 35 18. A process for diagnosing a disease or a susceptibility to a disease in a subject related to expression or activity of the IGS1 polypeptide of claim 13 in a subject comprising:
- (a) determining the presence or absence of a mutation in the nucleotide sequence encoding said IGS1 polypeptide in the genome of said subject; and/or

- (b) analyzing for the presence or amount of the IGS1 polypeptide expression in a sample derived from said subject.
19. A method for identifying agonists to the IGS1 polypeptide of claim 13 comprising:
- 5 (a) contacting a cell which produces a IGS1 polypeptide with a test compound; and
- (b) determining whether the test compound effects a signal generated by activation of the IGS1 polypeptide.
20. An agonist identified by the method of claim 19.
- 10 21. The method for identifying antagonists to the IGS1 polypeptide of claim 13 comprising:
- (a) contacting a cell which produces a IGS1 polypeptide with an agonist; and
- (b) determining whether the signal generated by said agonist is diminished in the presence of a candidate compound.
- 15 22. An antagonist identified by the method of claim 21.
23. A recombinant host cell produced by a method of claim 12 or a membrane thereof expressing an IGS1 polypeptide.
- 20 24. A method of creating a genetically modified non-human animal comprising the steps of
- a) ligating the coding portion of a polynucleotide consisting essentially of a nucleic acid sequence encoding a protein having the amino acid sequence SEQ ID NO: 2 or a biologically active fragment thereof to a regulatory sequence which is capable
- 25 of driving high level gene expression or expression in a cell type in which the gene is not normally expressed in said animal; or
- b) engineering the coding portion of a polynucleotide consisting essentially of a nucleic acid sequence encoding a protein having the amino acid sequence SEQ ID NO: 2 or a biologically active fragment thereof and reintroducing said sequence
- 30 in the genome of said animal in such a way that the endogenous gene alleles encoding a protein having the amino acid sequence SEQ ID NO: 2 or a biologically active fragment are fully or partially inactivated.